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L1          19 PROSTATE(W) CANCER AND (ESTRADIOL OR ESTROGEN?) AND MICROGRAM?
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=> dup rem l1  
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L2          19 DUP REM L1 (0 DUPLICATES REMOVED)
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=> dis ibib abs 12 1-19

L2 ANSWER 1 OF 19 MEDLINE on STN
 ACCESSION NUMBER: 2001133426 MEDLINE
 DOCUMENT NUMBER:
 TITLE: Developmental exposure to estrogens alters epithelial cell adhesion and gap junction proteins in the adult rat prostate.
 AUTHOR: Habermann H; Chang W Y; Birch L; Mehta P; Prins G S
 CORPORATE SOURCE: Department of Urology, University of Illinois, Chicago, Illinois 60612, USA.
 CONTRACT NUMBER: CA-73769 (United States NCI NIH HHS)
 DK 09873 (United States NIDDK NIH HHS)
 DK 40890 (United States NIDDK NIH HHS)
 SOURCE: Endocrinology, (2001 Jan) Vol. 142, No. 1, pp. 359-69.
 Journal code: 0375040. ISSN: 0013-7227.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 (RESEARCH SUPPORT, NON-U.S. GOV'T)
 (RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)
 (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
 LANGUAGE: English
 FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
 ENTRY MONTH: 200103
 ENTRY DATE: Entered STN: 4 Apr 2001
 Last Updated on STN: 4 Apr 2001
 Entered Medline: 1 Mar 2001
 AB Brief exposure to estrogens during the neonatal period

interrupts rat prostatic development by reducing branching morphogenesis and by blocking epithelial cells from entering a normal differentiation pathway. Upon aging, ventral prostates exhibit extensive hyperplasia and dysplasia suggesting that neonatal estrogens may predispose the prostate gland to preneoplastic lesions. To determine whether these prostatic lesions may be manifested through aberrant cell-to-cell communications, the present study examined specific gap junction proteins, Connexins (Cx) 32, and Cx 43, and the cell adhesion molecule, E-cadherin, in the developing, adult and aged rat prostate gland. Male rat pups were given 25 microgram estradiol benzoate or oil on days 1, 3, and 5 of life. Prostates were removed on days 1, 4, 5, 6, 10, 15, 30, or 90 or at 16 months, and frozen sections were immunostained for E-cadherin, Cx 43, and Cx 32. Colocalization studies were performed with immunofluorescence using specific antibodies for cell markers. Gap junctions in undifferentiated epithelial cells at days 1-10 of life were composed of Cx 43, which always colocalized with basal cell cytokeratins (CK 5/15). Cx 32 expression was first observed between days 10-15 and colocalized to differentiated luminal cells (CK 8/18). Cx 43 and Cx 32 never colocalized to the same cell indicating that gap junction intercellular communication differs between basal and luminal prostatic cells. While epithelial connexin expression was not initially altered in the developing prostates following estrogen exposure, adult prostates of neonatally estrogenized rats exhibited a marked decrease in Cx 32 staining and an increased proportion of Cx 43 expressing cells. In the developing prostate, E-cadherin was localized to lateral surfaces of undifferentiated epithelial cells and staining intensity increased as the cells differentiated into luminal cells. By day 30, estrogenized prostates had small foci of epithelial cells that did not immunostain for E-cadherins. In the adult and aged prostates of estrogenized rats, larger foci with differentiation defects and dysplasia were associated with a decrease or loss in E-cadherin staining. The present findings suggest that estrogen-induced changes in the expression of E-cadherin, Cx32 and Cx43 may result in impaired cell-cell adhesion and defective cell-cell communication and may be one of the key mechanisms through which changes toward a dysplastic state are mediated. These findings are significant in light of the data on human prostate cancers where carcinogenesis and progression are associated with loss of E-cadherin and a switch from Cx32 to Cx43 expression in the epithelium.

L2 ANSWER 2 OF 19 MEDLINE on STN
ACCESSION NUMBER: 1997001294 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8844286
TITLE: Aromatase mRNA levels in benign prostatic hyperplasia and prostate cancer.
AUTHOR: Tsugaya M; Harada N; Tozawa K; Yamada Y; Hayashi Y; Tanaka S; Maruyama K; Kohri K
CORPORATE SOURCE: Department of Urology, Nagoya City University, Medical School, Japan.
SOURCE: International journal of urology : official journal of the Japanese Urological Association, (1996 Jul) Vol. 3, No. 4, pp. 292-6.
Journal code: 9440237. ISSN: 0919-8172.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199612
ENTRY DATE: Entered STN: 28 Jan 1997
Last Updated on STN: 28 Jan 1997
Entered Medline: 30 Dec 1996
AB BACKGROUND: Estrogens are suspected to play a role in the

pathogenesis of benign prostatic hyperplasia (BPH) and prostate cancer. In this study, the expression of aromatase messenger ribonucleic acid (mRNA) was determined, and these levels were quantitated, in human prostatic tissues to evaluate the role of estrogens in the pathogenesis of BPH and prostate cancer. METHODS: Prostatic tissues were obtained either by retropubic prostatectomy, radical prostatectomy, or radical cystectomy from patients with BPH, prostate cancer, and bladder cancer. The expression of aromatase mRNA in the prostatic tissues was studied by Southern blot analysis of the reverse transcription and polymerase chain reaction technique (RT-PCR) products. Aromatase mRNA levels were measured in human prostatic tissues by the RT-PCR using a fluorescent primer. RESULTS: Aromatase mRNA was identified in all specimens by Southern blot analysis of the RT-PCR products. The concentrations of aromatase mRNA (mean +/- SD) which were measured by fluorometric quantitation in 16 of 19 patients with BPH and in 3 of 4 patients with prostate cancer, were 1.81 +/- 3.02, and 0.84 +/- 0.27, x 10(-3) attomoles/micrograms of total RNA, respectively. CONCLUSIONS: These results demonstrate local formation of estrogen in the prostates of patients with BPH and prostate cancer. Controlled studies will be necessary to determine whether this may be a factor in the development of BPH and prostate cancer.

L2 ANSWER 3 OF 19 MEDLINE on STN
ACCESSION NUMBER: 1997029194 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8875206
TITLE: Animal models for the preneoplastic lesions of the prostate.
AUTHOR: Pylkkänen L; Makela S; Santti R
CORPORATE SOURCE: Department of Radiotherapy and Oncology, University of Turku, Finland.
SOURCE: European urology, (1996) Vol. 30, No. 2, pp. 243-8. Ref:
33
JOURNAL code: 7512719. ISSN: 0302-2838.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199701
ENTRY DATE: Entered STN: 28 Jan 1997
Last Updated on STN: 28 Jan 1997
Entered Medline: 16 Jan 1997

AB OBJECTIVES: Reliable and adequate animal models are required, not only for investigation of etiology, pathogenesis, and treatment of prostate cancer, but also for chemoprevention of prostatic carcinogenesis. METHODS: Animal models for the study of premalignant changes in the prostate are reviewed in the paper, with specific reference to the neonatally estrogenized mouse model. RESULTS: Neonatal treatment of newborn Han:NMRI mice with synthetic non-steroidal estrogen, diethylstilbestrol (DES, 2 micrograms/pup on days 1-3 after birth) promoted hyperplastic and dysplastic changes in the periurethral region of the prostate at the age of 9-18 months. Dietary soy partially inhibited the development of prostatic dysplasia in these neonatally estrogenized animals, which may be due to phytoestrogens contained in soy-rich food. CONCLUSION: Prostatic cancer and its possible precursors develop spontaneously, or can be induced by different chemical and hormonal manipulations in certain animal species and strains. Neonatal estrogenization of the mouse results in prostatic dysplasia, which can be partially prevented by dietary soy. There are morphological similarities between human prostatic intraepithelial neoplasia (PIN) and dysplastic changes in rodent

prostates, but more data is needed before these dysplastic lesions can be considered equivalent to human PIN.

L2 ANSWER 4 OF 19 MEDLINE on STN
ACCESSION NUMBER: 1995230784 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7714978
TITLE: Immediate estrogen or estramustine phosphate therapy versus deferred endocrine treatment in nonmetastatic prostate cancer: a randomized multicenter study with 15 years of followup. The South Sweden Prostate Cancer Study Group.
AUTHOR: Lundgren R; Nordle O; Josefsson K
CORPORATE SOURCE: Department of Urology, University Hospital, Lund, Sweden.
SOURCE: The Journal of urology, (1995 May) Vol. 153, No. 5, pp. 1580-6.
JOURNAL CODE: 0376374. ISSN: 0022-5347.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
(COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199505
ENTRY DATE: Entered STN: 24 May 1995
Last Updated on STN: 17 Jan 2003
Entered Medline: 12 May 1995
AB From November 1978 to July 1984, 285 men with previously untreated, localized prostate cancer were consecutively randomized in an open multicenter study. The main objective was to determine if early endocrine treatment prolongs the interval to metastasis and/or cancer related or overall survival. Patients were randomized to receive either 80 mg. polyestradiol phosphate by intramuscular injection every 4 weeks plus 50 micrograms ethinylestradiol 3 times daily or 280 mg. estramustine phosphate 2 times daily, or for surveillance only but with deferred endocrine treatment at progression to metastatic disease. From 1983 further inclusion into the polyestradiol phosphate plus ethinylestradiol group was closed because of a high frequency of cardiovascular complications and thereafter 13 patients were instead randomized to a new treatment group with 80 mg. polyestradiol phosphate only by intramuscular injection every 4 weeks. Mean age was 70 years for 228 evaluable patients: 66 in the polyestradiol phosphate plus ethinylestradiol group, 74 in the estramustine phosphate group and 88 in the deferred treatment group, respectively. Mean followup for 100 patients alive on August 31, 1993 was 144 months (range 111 to 180). During the observation period 51 patients had metastasis. There was no difference in interval to metastasis ($p = 0.07$) among the 3 groups, although there was a tendency for a higher probability of metastases in the deferred treatment group. A total of 128 patients (56%) died during the observation period and prostatic cancer was considered to be the cause of death in 46 (20%). There was a significant difference ($p = 0.03$) among the 3 groups in the probability of dying of prostatic cancer, with the highest risk in the surveillance group but we found no significant difference in overall survival. The relevance of different prognostic factors and their interaction with treatment was also evaluated. These analyses were applied to the entire patient group as well as to the different subgroups. We found that patients with moderately well differentiated cancer (stage greater than T0a) who received early treatment with estramustine phosphate had the lowest risk of metastases or death from prostatic cancer, while those with well differentiated cancer

(stage greater than T0a) did best on early polyestradiol phosphate plus ethinylestradiol treatment.

L2 ANSWER 5 OF 19 MEDLINE on STN
ACCESSION NUMBER: 1996035019 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7554242
TITLE: Quantification of creatine kinase BB isoenzyme in tumor cytosols and serum with an ultrasensitive time-resolved immunofluorometric technique.
AUTHOR: Zarghami N; Yu H; Diamandis E P; Sutherland D J
CORPORATE SOURCE: Department of Clinical Biochemistry, Toronto Western Division, Toronto Hospital, Ontario, Canada.
SOURCE: Clinical biochemistry, (1995 Jun) Vol. 28, No. 3, pp. 243-53.
JOURNAL CODE: 0133660. ISSN: 0009-9120.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199511
ENTRY DATE: Entered STN: 27 Dec 1995
Last Updated on STN: 27 Dec 1995
Entered Medline: 7 Nov 1995
AB OBJECTIVES: To develop a highly sensitive immunofluorometric procedure for creatine kinase BB isoenzyme and use it to measure CK-BB in tumor cytosolic extracts and serum of cancer patients and healthy volunteers.
DESIGN AND METHODS: For assay development, we used two monoclonal antibodies in combination with time-resolved fluorometry and the biotin-avidin system. We measured CK-BB in breast tumor cytosols and studied its association with steroid hormone receptors. We also measured CK-BB in the serum of healthy subjects and patients with prostate cancer. We have examined the molecular weight of CK-BB in serum using high performance liquid chromatography. RESULTS: The evaluation of the method revealed good precision and accuracy. Study of 336 breast tumor cytosols and 9 normal breast cytosols has shown that CK-BB is overexpressed by 95% of breast tumors and that CK-BB is present in its 80 kDa form. A close association between CK-BB and estrogen but not progesterone receptors was found, suggesting that CK-BB overexpression is another marker of estrogen sensitivity of these tumors. Previous studies, using CK-BB radioimmunoassay could not detect CK-BB in the serum of about 50% of healthy subjects. We have assessed CK-BB levels in 80 male volunteers, detected CK-BB in all sera and provided a detailed distribution of values. We further demonstrated that 30% of prostate cancer patients in remission (PSA < 0.4 microgram/L) post radical prostatectomy and 50% of patients with active prostate cancer (PSA > 20 microgram /L) have elevated serum CK-BB levels. The patients with highly elevated CK-BB also had highly elevated serum PSA. We have demonstrated that some patients who have elevated serum CK-BB also have macromolecular CK complexes in their serum with molecular weights of 700 and 350 kDa as well as the 80 kDa CK-BB isoenzyme. Only the latter was recognized by the assay developed. CONCLUSIONS: CK-BB is a marker of estrogen sensitivity in breast cancer; Patients with prostate cancer have elevated CK-BB in their serum; The new highly specific and sensitive assay may be further used to study the role of CK-BB in various malignancies.

L2 ANSWER 6 OF 19 MEDLINE on STN
ACCESSION NUMBER: 1994336429 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8058523
TITLE: Soy intake and cancer risk: a review of the in vitro and in

vivo data.

AUTHOR: Messina M J; Persky V; Setchell K D; Barnes S
CORPORATE SOURCE: National Cancer Institute, National Institutes of Health, Bethesda, MD.
SOURCE: Nutrition and cancer, (1994) Vol. 21, No. 2, pp. 113-31.
Ref: 112
Journal code: 7905040. ISSN: 0163-5581.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Space Life Sciences
ENTRY MONTH: 199409
ENTRY DATE: Entered STN: 20 Sep 1994
Last Updated on STN: 6 Feb 1998
Entered Medline: 13 Sep 1994

AB International variations in cancer rates have been attributed, at least in part, to differences in dietary intake. Recently, it has been suggested that consumption of soyfoods may contribute to the relatively low rates of breast, colon, and prostate cancers in countries such as China and Japan. Soybeans contain a number of anticarcinogens, and a recent National Cancer Institute workshop recommended that the role of soyfoods in cancer prevention be investigated. In this review, the hypothesis that soy intake reduces cancer risk is considered by examining relevant *in vitro*, animal, and epidemiological data. Soybeans are a unique dietary source of the isoflavone genistein, which possesses weak estrogenic activity and has been shown to act in animal models as an antiestrogen. Genistein is also a specific inhibitor of protein tyrosine kinases; it also inhibits DNA topoisomerases and other critical enzymes involved in signal transduction. *In vitro*, genistein suppresses the growth of a wide range of cancer cells, with IC₅₀ values ranging from 5 to 40 microM (1-10 micrograms/ml). Of the 26 animal studies of experimental carcinogenesis in which diets containing soy or soybean isoflavones were employed, 17 (65%) reported protective effects. No studies reported soy intake increased tumor development. The epidemiological data are also inconsistent, although consumption of nonfermented soy products, such as soymilk and tofu, tended to be either protective or not associated with cancer risk; however, no consistent pattern was evident with the fermented soy products, such as miso. Protective effects were observed for both hormone- and nonhormone-related cancers. While a definitive statement that soy reduces cancer risk cannot be made at this time, there is sufficient evidence of a protective effect to warrant continued investigation.

L2 ANSWER 7 OF 19 MEDLINE on STN
ACCESSION NUMBER: 1993268675 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8497428
TITLE: Genistein and biochanin A inhibit the growth of human prostate cancer cells but not epidermal growth factor receptor tyrosine autophosphorylation.
AUTHOR: Peterson G; Barnes S
CORPORATE SOURCE: Department of Biochemistry, University of Alabama, Birmingham 35294-0019.
SOURCE: The Prostate, (1993) Vol. 22, No. 4, pp. 335-45.
Journal code: 8101368. ISSN: 0270-4137.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199306
ENTRY DATE: Entered STN: 2 Jul 1993
Last Updated on STN: 3 Mar 2000

Entered Medline: 23 Jun 1993

AB The effect of the isoflavones, genistein, daidzein, and biochanin A on the growth of the LNCaP and DU-145 human prostate cancer cell lines has been examined. Genistein and biochanin A, but not daidzein, inhibit both serum and EGF-stimulated growth of LNCaP and DU-145 cells (IC₅₀ values from 8.0 to 27 micrograms/ml for serum and 4.3 to 15 micrograms/ml for EGF), but have no significant effect of the EGF receptor tyrosine autophosphorylation. In contrast, tyrphostin 25, a specific EGF receptor tyrosine kinase inhibitor, inhibits EGF-stimulated growth and EGF receptor tyrosine autophosphorylation in these whole cells, but does not inhibit serum-stimulated growth. These data suggest that the mechanism of action of genistein and biochanin A does not depend on inhibition of EGF receptor tyrosine autophosphorylation, but on a more distal event in the EGF receptor-mediated signal transduction cascade.

L2 ANSWER 8 OF 19 MEDLINE on STN
ACCESSION NUMBER: 1991148122 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1997702
TITLE: Primary orchiectomy versus estrogen therapy in advanced prostatic cancer—a randomized study: results after 7 to 10 years of followup.
AUTHOR: Johansson J E; Andersson S O; Holmberg L; Bergstrom R
CORPORATE SOURCE: Department of Urology, Orebro Medical Center Hospital, Sweden.
SOURCE: The Journal of urology, (1991 Mar) Vol. 145, No. 3, pp. 519-22; discussion 522-3.
Journal code: 0376374. ISSN: 0022-5347.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
(COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199104
ENTRY DATE: Entered STN: 19 Apr 1991
Last Updated on STN: 19 Apr 1991
Entered Medline: 1 Apr 1991

AB Of 163 new consecutively diagnosed cases of advanced (T3-4 M0 or T04M1) prostatic cancer 13 had contraindications for estrogen treatment, and the remainder were randomized to orchiectomy (76) or to estrogen treatment (74), consisting of 150 micrograms ethinyl estradiol daily and 80 mg. polyestradiol monthly. During the followup period of 7 to 10 years disease progression was noted in 27 patients (36%) treated with estrogen and 39 (51%) orchiectomized patients. The free of progression survival rate was significantly better (less than 0.05) among the estrogen treated patients but the over-all survival rates after orchiectomy and estrogen treatment were almost identical. A significantly higher frequency of cardiovascular side effects was noted in the estrogen group (23 cases) compared to the orchiectomy group (4 cases). Therefore, estrogen treatment in this form cannot be recommended for the palliative treatment of prostate cancer.

L2 ANSWER 9 OF 19 MEDLINE on STN
ACCESSION NUMBER: 1991243598 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1709853
TITLE: Goserelin. A review of its pharmacodynamic and pharmacokinetic properties, and clinical use in sex hormone-related conditions.

AUTHOR: Chrisp P; Goo K L
CORPORATE SOURCE: Adis Drug Information Services, Auckland, New Zealand.
SOURCE: Drugs, (1991 Feb) Vol. 41, No. 2, pp. 254-88. Ref: 155
Journal code: 7600076. ISSN: 0012-6667.

PUB. COUNTRY: New Zealand
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199107
ENTRY DATE: Entered STN: 19 Jul 1991
Last Updated on STN: 3 Mar 2000
Entered Medline: 2 Jul 1991

AB Goserelin is a synthetic analogue of gonadotrophin-releasing hormone (GnRH) [luteinising hormone-releasing hormone (LHRH); or gonadorelin] which stimulates gonadotrophin and sex hormone release in the short term, and then causes suppression with continued administration. Goserelin is given as a subcutaneous biodegradable depot incorporating 3.6 mg of the drug, which is released continuously at an average rate of 120 micrograms/day over 4 weeks. Monthly goserelin depot therapy produces partial disease remission or stabilisation in about 75% of men with previously untreated prostatic cancer, a rate equivalent to that achieved with orchidectomy or diethylstilbestrol (stilboestrol). The response to goserelin is more rapid than to diethylstilbestrol, and goserelin is better tolerated. About 30 to 45% of premenopausal women with breast cancer responded to goserelin using objective assessment criteria, suggesting comparability to ovariectomy. In benign hormone-dependent conditions, preoperative goserelin aids surgical removal of uterine leiomyoma (fibroids) and reduces blood loss, and 6 months of therapy relieves the signs and symptoms of endometriosis. The elevation in testosterone at the beginning of goserelin therapy can result in disease 'flare' in men with prostate cancer, and sex steroid suppression with continued treatment results in hot flushes and loss of libido in most patients. Thus, goserelin is an effective alternative to surgery or estrogen therapy in prostatic cancer palliation, and possibly to ovariectomy in premenopausal breast cancer. Other gynaecological conditions reliant on the pituitary-gonadal axis also appear amenable to hormone manipulation with goserelin.

L2 ANSWER 10 OF 19 MEDLINE on STN
ACCESSION NUMBER: 1988155402 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3126294
TITLE: One-month release injectable microcapsules of a luteinizing hormone-releasing hormone agonist (leuprolide acetate) for treating experimental endometriosis in rats.
AUTHOR: Okada H; Heya T; Ogawa Y; Shimamoto T
CORPORATE SOURCE: Central Research Division, Takeda Chemical Industries, Ltd., Osaka, Japan.
SOURCE: The Journal of pharmacology and experimental therapeutics, (1988 Feb) Vol. 244, No. 2, pp. 744-50.
Journal code: 0376362. ISSN: 0022-3565.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198804
ENTRY DATE: Entered STN: 8 Mar 1990
Last Updated on STN: 8 Mar 1990
Entered Medline: 12 Apr 1988

AB Leuprolide acetate is a highly potent analog of luteinizing hormone-releasing hormone. We have prepared 1-month release injectable microcapsules of leuprolide acetate using a biodegradable polymer, poly

(dl-lactide-co-glycolide), to treat an endocrine-dependent tumor, prostate cancer. In the present study, the possibility using the microcapsules to treat endometriosis was investigated. In rats, the microcapsules exhibited a pseudo-zero order release from the injection site for 1 month after being administered s.c. and i.m., and maintained effective constant serum levels of the analog during the 4-week treatment. A single injection of the microcapsules (100 micrograms/kg/day as leuprolide acetate) suppressed luteinizing hormone, follicle-stimulating hormone and estradiol for more than 4 weeks, and caused a dramatic regression of growth of Jones experimental endometriosis model in female rats. These results encourage the belief that a 1-month release parenteral preparation of leuprolide acetate may be potentially useful in the therapy of endometriosis in human beings.

L2 ANSWER 11 OF 19 MEDLINE on STN
ACCESSION NUMBER: 1989205445 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2468281
TITLE: Aspects on reference values for tumor markers in human prostatic carcinoma.
AUTHOR: Ekman P; Lewenhaupt A; Eneroth P; Kallner A
CORPORATE SOURCE: Department of Urology, Karolinska Hospital, Stockholm, Sweden.
SOURCE: American journal of clinical oncology, (1988) Vol. 11 Suppl 2, pp. S80-2.
Journal code: 8207754. ISSN: 0277-3732.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198905
ENTRY DATE: Entered STN: 6 Mar 1990
Last Updated on STN: 6 Feb 1998
Entered Medline: 15 May 1989

AB The efficiency of the tumor markers prostatic acid phosphatase (PAP), prostate-specific antigen (PSA), neopterin, and osteocalcin was tested with regard to their ability to predict cancer death within 2 years plus survival beyond 2 years in a series of patients with newly diagnosed prostate cancer. For all markers, an elevated level suggested a tumor with a worse prognosis. Moreover, the extent to which the level was increased carried additional information. The prognostic efficiency was routinely improved by selecting cutoff levels higher than the standards suggested by the radioimmunoassay (RIA) kit manufacturers. Seventy-four percent of the patients with elevated levels of neopterin were still alive after 2 years when 8 nmol/L was selected as the upper normal value compared to only 43% at 12 nmol/L. At a cut-off value of 3 micrograms/L for osteocalcin, 79% of the patients with elevated levels were still alive after 2 years compared with only 20% when 7 micrograms/L was selected. Such adjustments to higher cutoff levels could be made without increasing the number of "false-negatives." The efficiency of PAP to predict short-term prognosis was poor at the standard cutoff level of 1.9 microgram/L. Not until 20 micrograms/L was selected did the efficiency exceed 80%. PSA was highly sensitive but little specific at any of the cutoff levels tested with regard to ability to indicate prognosis.

L2 ANSWER 12 OF 19 MEDLINE on STN
ACCESSION NUMBER: 1988335849 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3420036
TITLE: Efficacy and advantages in the use of low doses of Anandron and estrogen combination in the treatment of prostate cancer.

AUTHOR: Rao B R; Geldof A A; van der Wilt C L; de Voogt H J
CORPORATE SOURCE: Department of Endocrinology, Academisch Ziekenhuis Vrije
Universiteit, Amsterdam, The Netherlands.
SOURCE: The Prostate, (1988) Vol. 13, No. 1, pp. 69-78.
Journal code: 8101368. ISSN: 0270-4137.
PUB. COUNTRY: United States
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198810
ENTRY DATE: Entered STN: 8 Mar 1990
Last Updated on STN: 8 Mar 1990
Entered Medline: 26 Oct 1988
AB Treatment effects of RU 23908 antiandrogen (Anandron) and estrogen in low doses on hormone-dependent rat prostatic adenocarcinoma (R3327-H) were investigated. Tumor-bearing Copenhagen rats were treated for 6 weeks with 8 micrograms Anandron and 1 microgram estradiol-17 beta every two days. Reduction and counteraction of androgen synthesis and action was established by an observed decline in serum testosterone level and by changes in both histology and weight of androgen target organs. Prostate tumor growth rate was significantly retarded in rats treated with Anandron/Estradiol combination compared to untreated intact control and was equal to the slow growth rate in castrate tumor-bearing animals. Tumor histology changes during treatment correlated with the observed growth rate retardation. Areas of necrosis, metaplasia, and acelularity were more frequently observed in tumors of Anandron/Estradiol-treated compared to castrated rats. These results suggest that low doses of Anandron and estrogen can effectively be combined as a complete androgen counteracting therapy for hormone-dependent prostatic carcinoma with minimal undesired side effects.

L2 ANSWER 13 OF 19 MEDLINE on STN
ACCESSION NUMBER: 1986313308 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2944084
TITLE: Persistent blockade of the pituitary-gonadal axis in patients with prostatic carcinoma during chronic administration of D-Trp-6-LH-RH.
AUTHOR: Gonzalez-Barcena D; Perez-Sanchez P; Berea-Dominguez H; Graef-Sanchez A; Becerril-Morales M; Comaru-Schally A M; Schally A V
SOURCE: The Prostate, (1986) Vol. 9, No. 2, pp. 207-15.
Journal code: 8101368. ISSN: 0270-4137.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198610
ENTRY DATE: Entered STN: 21 Mar 1990
Last Updated on STN: 21 Mar 1990
Entered Medline: 6 Oct 1986
AB Forty patients with stage D2 prostatic carcinoma were treated for up to 30 months with D-Trp-6-LH-RH. The analog was given s.c. once daily at a dose of 1 mg/day for the first 7 days. Subsequently, the dose was reduced to 100 micrograms/day. In follow-up studies, 30 men continued this therapy for up to 24 months. Blood samples were taken before the injection of the analog and 1, 2, 4, and 6 hours later. Serum LH, FSH, and testosterone levels were measured by RIA every month for 2 years. The initial administration of 1 mg D-Trp-6-LH-RH caused a marked elevation of

LH and FSH, which lasted more than 24 hours. However, 1 month later and throughout the therapy, the basal values of LH and FSH were below the normal range and no increase in serum gonadotropins levels was obtained after administration of the analog. Initial plasma testosterone was within normal limits, but during treatment with D-Trp-6-LH-RH it fell to castration levels, and no increases were seen during the 6 hours following the injection of the analog. These results show that chronic administration of D-Trp-6-LH-RH, at the doses used, blocks the pituitary-gonadal axis and that the escape phenomenon from the effects of the LH-RH agonists-induced blockade does not occur under our conditions in contrast to observations of Kerle et al with the I.C.I. Analog 118630 (8). The accumulated results reinforce the view that long-term therapy with agonists of LH-RH is the preferred alternative to surgical castration or therapy with estrogens in men with metastatic prostate cancer.

L2 ANSWER 14 OF 19 MEDLINE on STN
ACCESSION NUMBER: 1986248152 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3087785
TITLE: Comparison of the efficacy of subcutaneous and nasal spray buserelin treatment in suppression of testicular steroidogenesis in men with prostate cancer.
AUTHOR: Rajfer J; Handelsman D J; Crum A; Steiner B; Peterson M; Swerdlow R S
CONTRACT NUMBER: RR00425 (United States NCRR NIH HHS)
SOURCE: Fertility and sterility, (1986 Jul) Vol. 46, No. 1, pp. 104-10.
Journal code: 0372772. ISSN: 0015-0282.
PUB. COUNTRY: United States
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198607
ENTRY DATE: Entered STN: 21 Mar 1990
Last Updated on STN: 3 Feb 1997
Entered Medline: 29 Jul 1986

AB The comparative efficacy of subcutaneous injections and intranasal spray in the maintenance of suppression of testicular function in men with advanced prostatic cancer treated with a gonadotropin-releasing hormone (GnRH) agonist, Buserelin, was evaluated in a nonrandomized clinical trial. After a common induction period of 1 week's treatment with 500 micrograms three times daily by subcutaneous injection, patients were allocated into one of two groups for maintenance therapy with either subcutaneous (200 micrograms once daily) or intranasal (400 micrograms nasal spray three times daily) Buserelin therapy. Plasma luteinizing hormone (LH) and sex steroid (testosterone [T], dihydrotestosterone [DHT], and estradiol [E2]) patterns were studied before the start and at days 1, 7, and 14 and months 2, 4, 6, and 12 on maintenance regimens. During the maintenance therapy, age-adjusted T levels were markedly suppressed to near-castrate levels in both treatment groups. Despite this marked suppression, age-adjusted T levels were consistently lower in men treated with the subcutaneous regimen from the 2nd week to the 12th month of treatment in morning pooled specimens as well as in detailed sampling over a 24-hour period after 12 months of continuous treatment. A similar pattern of enhanced suppression by the subcutaneous regimen was also observed for age-adjusted DHT, but not E2, levels during the study. Neither the magnitude nor the time course of T suppression by GnRH analog treatment could be entirely explained by the

nature of the decline in plasma LH levels, which fell much less and more gradually over a 12-month period.(ABSTRACT TRUNCATED AT 250 WORDS)

L2 ANSWER 15 OF 19 MEDLINE on STN
ACCESSION NUMBER: 1986064302 MEDLINE
DOCUMENT NUMBER: PubMed ID: 6242477
TITLE: Inhibition of the growth of some hormone dependent tumors by D-Trp6-LH-RH.
AUTHOR: Schally A V; Redding T W; Comaru-Schally A M
CONTRACT NUMBER: AM 07467 (United States NIADDK NIH HHS)
SOURCE: Medical oncology and tumor pharmacotherapy, (1984) Vol. 1, No. 2, pp. 109-18.
Journal code: 8405039. ISSN: 0736-0118.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198601
ENTRY DATE: Entered STN: 21 Mar 1990
Last Updated on STN: 3 Feb 1997
Entered Medline: 14 Jan 1986

AB We have investigated the effects of chronic administration of D-Trp6-LH-RH on the growth of various hormone dependent tumors in rats and mice. Treatment of male Copenhagen F-1 rats bearing the Dunning R-3327H prostate adenocarcinoma with 25 micrograms of D-Trp6-LH-RH bid for 21 days significantly reduced tumor weight and volume as compared to controls. Serum LH, prolactin and testosterone levels in Copenhagen F-1 rats bearing Dunning tumors were significantly decreased after treatment with D-Trp6-LH-RH. Administration of D-Trp6-LH-RH in doses of 25 micrograms/day for 21 days to mice bearing the MXT mammary carcinoma significantly decreased tumor weight and volume. In rats bearing the MT/W9A mammary adenocarcinoma, D-Trp6-LH-RH, at a dose of 25 micrograms bid for 28 days significantly decreased tumor weight and volume. Administration of D-Trp6-LH-RH in a dose of 25 micrograms/day, 3-18 days after inoculation with the tumor, inhibited the growth of the prolactin (PRL) and ACTH-secreting pituitary tumor 7315a in female Buffalo rats. In three experiments D-Trp6-LH-RH (30-60 micrograms/day) decreased tumor weight and/or volume of the Swarm chondrosarcoma. Regression of these hormone-dependent tumors in rats and mice in response to chronic administration of D-Trp6-LH-RH suggests that this compound can be used for treatment of prostate cancer and breast cancer, and also considered for the development of a new endocrine therapy for chondrosarcomas, osteosarcomas, pituitary tumors and other hormone-dependent neoplasias. The demonstration of the successful use of LH-RH agonists for the palliative management of stage C and D prostate cancer has already shown that this treatment could be employed instead of surgical orchiectomy or estrogen therapy. Preliminary clinical trials suggest that agonists of LH-RH might also be of help in the treatment of breast cancer in premenopausal women.

L2 ANSWER 16 OF 19 MEDLINE on STN
ACCESSION NUMBER: 1983295860 MEDLINE
DOCUMENT NUMBER: PubMed ID: 6411994
TITLE: Suppression of testicular steroidogenesis by the GnRH agonistic analogue Buserelin (HOE-766) in patients with prostatic cancer: studies in relation to dose and route of administration.
AUTHOR: Tolis G; Faure N; Koutsilieris M; Lemay A; Klioze S; Yakabow A; Fazekas A T

SOURCE: Journal of steroid biochemistry, (1983 Jul) Vol. 19, No. 1C, pp. 995-8.
Journal code: 0260125. ISSN: 0022-4731.

PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 198310

ENTRY DATE: Entered STN: 19 Mar 1990
Last Updated on STN: 19 Mar 1990
Entered Medline: 8 Oct 1983

AB Forty-six patients with prostatic carcinoma received the gonadotropin releasing hormone agonistic analogue (GnRH-A) Buserelin at doses ranging from 0.05 to 1.5 mg subcutaneously and/or 0.4 to 1.2 mg intranasally (i.n.) daily for 12-120 weeks. An increase in plasma testosterone (T) was seen in 15% of patients on day 7 of therapy; with continuation of treatment plasma T as well as DHT and E2 levels fell by more than 50% within 2-4 weeks in those patients receiving greater than or equal to 50 micrograms s.c. and/or greater than or equal to 1 mg in daily dose. Persistently low plasma T levels (less than 1 ng/ml) were reached in 60% of patients receiving 50 micrograms s.c. in 89% of those treated with 1.2 mg i.n. and in 100% of patients who received initially 1.5 mg s.c. X 7 days followed by 1.2 mg i.n. daily. The above data indicate the importance of dose and route of administration in achieving significant suppression of plasma sex steroids in patients with prostate cancer in whom Buserelin can be used as an alternative to castration or estrogens.

L2 ANSWER 17 OF 19 MEDLINE on STN
ACCESSION NUMBER: 1984081288 MEDLINE
DOCUMENT NUMBER: PubMed ID: 6418264
TITLE: Treatment of advanced prostatic cancer with buserelin, an analogue of gonadotrophin releasing hormone.
AUTHOR: Waxman J H; Wass J A; Hendry W F; Whitfield H N; Bary P;
Besser G M; Malpas J S; Oliver R T
SOURCE: British journal of urology, (1983 Dec) Vol. 55, No. 6, pp. 737-42.
Journal code: 15740090R. ISSN: 0007-1331.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: (CLINICAL TRIAL)
LANGUAGE: English
FILE SEGMENT: Journal; Article; (JOURNAL ARTICLE)
ENTRY MONTH: 198402
ENTRY DATE: Entered STN: 19 Mar 1990
Last Updated on STN: 19 Mar 1990
Entered Medline: 14 Feb 1984

AB Twenty-two consecutive patients with newly diagnosed symptomatic, locally advanced or metastatic prostate cancer were treated with intranasal buserelin, a long-acting analogue of gonadotrophin releasing hormone, in divided dosages of between 600 and 1000 micrograms daily. Suppression of testosterone occurred in 1 of 5 patients treated with 600 micrograms daily and in all 17 patients receiving 1000 micrograms daily. Two of 5 patients treated with the 600 micrograms regimen and 16 of 17 patients receiving the 1000 micrograms regimen showed subjective and objective evidence of disease regression. Follow-up was from 1 to 16 months (mean 7.1 months); 6 patients have relapsed during this period. Buserelin offers an effective alternative medical treatment of carcinoma of the prostate and, apart from impotence, does not have the side effects of oestrogens.

L2 ANSWER 18 OF 19 MEDLINE on STN
ACCESSION NUMBER: 1982261542 MEDLINE
DOCUMENT NUMBER: PubMed ID: 6179769
TITLE: Clinical study on increased serum thyroxine-binding globulin in cancerous state.
AUTHOR: Kajita Y; Ishida M; Hachiya T; Miyazaki T; Yoshimura M; Ijichi H; Ochi Y
SOURCE: Endocrinologia japonica, (1981 Dec) Vol. 28, No. 6, pp. 785-91.
Journal code: 0376546. ISSN: 0013-7219.
PUB. COUNTRY: Japan
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198210
ENTRY DATE: Entered STN: 17 Mar 1990
Last Updated on STN: 17 Mar 1990
Entered Medline: 12 Oct 1982

AB Serum thyroxine-binding globulin (TBG) in 169 patients with various cancers was determined by radioimmunoassay (RIA). Eleven patients showed a high serum TBG level (greater than 35 micrograms/ml). Two of them had been treated with estrogen for prostate cancer. One patient had high serum TBG with serum hepatitis. Another 8 cases had normal liver function and also normal levels serum estrogen. Thus, about 4.7% (8/169) of the cancer patients had high serum TBG and mild hyperthyroxinemia caused by unknown mechanisms. The high TBG level in these patients continued until just before death, or in some cases decreased to normal after removal of cancer tumors by operation. Cancer is occasionally associated with an increase in serum TBG. Although the mechanism is not clear, the increased TBG in the cancerous state is interesting and has significance as a tumor marker.

L2 ANSWER 19 OF 19 MEDLINE on STN
ACCESSION NUMBER: 1980251870 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7190620
TITLE: Effects of diethylstilbestrol and estramustine phosphate on serum sex hormone binding globulin and testosterone levels in prostate cancer patients.
AUTHOR: Karr J P; Wajsman Z; Kirdani R Y; Murphy G P; Sandberg A A
SOURCE: The Journal of urology, (1980 Aug) Vol. 124, No. 2, pp. 232-6.
Journal code: 0376374. ISSN: 0022-5347.
Report No.: PIP-801385; POP-00079664.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals;
Population
ENTRY MONTH: 198010
ENTRY DATE: Entered STN: 15 Mar 1990
Last Updated on STN: 1 Nov 2002
Entered Medline: 21 Oct 1980

AB Serum testosterone-estradiol binding globulin and total testosterone were measured in 2 groups of male controls (less than 50 and more than 65 years old) and in 7 groups of prostatic cancer patients treated with various endocrine manipulation procedures, including orchectomy, and estramustine phosphate and diethylstilbestrol therapy. There were 133 individuals studied. Total serum testosterone levels were significantly higher in the younger versus the older control group and testosterone-estradiol binding globulin levels were

significantly higher in the older men. Whereas orchiectomy reduced serum testosterone to low concentrations (72 plus or minus 11 ng. per 100 ml.) testosterone-estradiol binding globulin levels were not altered. In contrast, estramustine phosphate and diethylstilbestrol therapy, when administered to intact or castrated patients, resulted in depressed testosterone and markedly elevated testosterone-estradiol binding globulin serum levels, particularly in those patients receiving estramustine phosphate (less than 35 ng. per 100 ml. and more than 6 micrograms per 100 ml., respectively). These studies led to the conclusion that diethylstilbestrol or estramustine phosphate therapy is significantly more effective than orchiectomy in eliciting a concomitant elevation of testosterone-estradiol binding globulin and a depression of total testosterone. Even though free serum testosterone was not measured in the present study the law of mass action would indicate that in those patients with high testosterone-estradiol binding globulin (more than 5 microgram. per 100 ml.) and low total testosterone levels (less than 80 ng. per 100 ml.) the availability of biologically active (unbound steroid) testosterone would be negligible. This study attempted to determine whether oral administration of diethylstilbestrol (DES) or estramustine phosphate, a mustard compound derivative with unknown mechanism of action, is as effective in the treatment of prostate cancer as castration. Serum testosterone-estradiol binding globulin and total testosterone were measured in 2 groups of male controls (aged under 50 years or over 65 years) and in 7 groups of prostatic cancer patients treated by endocrine manipulation, including orchiectomy and DES or estramustine phosphate. 133 persons were studied. Total serum testosterone levels were significantly higher in younger vs. older controls and testosterone-estradiol binding globulin levels were significantly higher in the older men. Although orchiectomy reduced serum testosterone to low concentrations, the binding globulin level was not altered by surgery. In contrast, estramustine phosphate and DES therapy, administered to intact or castrated patients, led to depressed testosterone and markedly elevated binding globulin levels in serum; this effect was most pronounced among estramustine phosphate users. Therefore, it is concluded that DES or estramustine phosphate therapy is significantly more effective than orchiectomy in eliciting concomitant elevation of the testosterone-estradiol binding globulin and a depression of total testosterone.

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(ESTRADIOL OR ESTROGEN?) AND MICROGRAM?
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| FULL ESTIMATED COST | 0.56 | 25.91 |

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